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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,367	09/16/2005	George L Wright JR.	113019.159US1	7128

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
01/15/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/505,367	WRIGHT ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/9/05 3/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-46 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27, 29, 30. 33-35, 43 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear how claim 27 further limits claim 22. Claim 22 requires the three markers of EP2, EP3 and EP6. Claim 27 states that the sample comprises at least two markers

Claim 29 is vague and indefinite in referring to itself. for purpose of examination, claim 29 will be read as dependent on claim 28.

The recitation of "protein" in claims 43 and 44 lacks specific antecedence basis in claim 42

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 42-44 are drawn to purified markers EP1 to EP14 characterized only by a molecular weight range. Claims 45 and 46 are drawn to kits comprising said markers. Claims 1-

41 are drawn to method claims reliant on the identity of said markers. When given the broadest reasonable interpretation, the term biomarker includes full length neutral peptides and proteins. With the exception of EP1 and EP3 which are taught by the specification to be alpha defensin 1 and 2, respectively (page 49, lines 18-19 and page 48, lines 25-28), the specification describes only ions detected by mass spectrometry having the mass to charge ratios reflected in the claims. It is well known in the art of mass spectrometry that molecules fragment in the process of acquiring a charge, and that some detectable ions having a specific mass to charge ratio are actually twice the mass but have acquired a dual charge. Thus, it is reasonable to assume that the mass to charge ratios detected by mass spectrometry do not represent a "molecular ion" with a single charge of one. Therefore the specification fails to adequately describe EP2 and EP4-14 as actual biomarkers rather than reactive ions generated in the mass spectrometer. It logically follows that the method claims reliant on the biomarkers are also no adequately described. amendment of claims 1 and 25 to qualify the recited molecular weights as mass to charge ratios will over come this rejection for claims 1-41.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25, 26, 32, 36-38, 41, 45 and 46 are rejected under 35 U.S.C. 102(a) as being anticipated by Vlahou et al (American Journal of Pathology, April 2001, Vol. 158, pp. 1491-1502, reference of the IDS filed Nov., 9, 2005).

Vlahou et al disclose a method for detecting the marker EP1 in a urine sample by gas phase ion spectrometry by SELDI (Figures 1 and 2). Vlahou et al disclose nickel IMAC3 chip array for the processing of lysates from microdissected cells (page 1493, second column, under the heading "ProteinChip SELDI Analysis of Cell Lysates") and a SELDI immunoassay (page 1494, second column "Immunoassay"). Vlahou et al disclose that the 3.432 SD 24.4 marker was a marker for urinary bladder cancer (page 1495, second column, lines 24-29). Vlahou et al isolate the 3.432 SD 24.4 protein identified as defensin (page 1496, Figure 4). 3.432 SD 24.4 disclose instructions for how to contact a sample with the marker (page 1493 "ProteinChip SELDI Analysis" and page 1494, "Immunoassay" therefore fulfilling the specific embodiment of clams 45 and 46 requiring instructions in "including methods for contacting a sample comprising the marker with the adsorbent. Vlahou et al fulfill the specific limitations of claims 43 and 44 because claims 43 and 44 are product by process claims the characterized by the attributes of the product.

Claims 45 and 46 rejected under 35 U.S.C. 102(b) as being anticipated by Sulkowski (Trends in Biotechnology, 1985, Vol. 3, pp. 1-7).

Sulkowski disclose immobilized metal affinity chromatography, and thus fulfills the limitations of an adsorbent attached to a substrate. It is inherent in the properties of the adsorbent that it would be suitable for retaining the markers listed in claim 45. Sulkowski discloses that peptides containing cysteine, histidine and arginine can donate electrons to form a complex with the immobilized metal ions (pages 1-2 under "background information"). Sulkowski disclose instructions for adsorbing proteins and eluting proteins from the IMAC (pages 2-3, "Some Dos and Dont's of IMAC") which would apply to the markers recited in claim 45.

Claims 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Chertov et al (Journal of Biological Chemistry, 1996, Vol. 271, pp. 2935-2940).

Chertov et al disclose the isolated defensins of HNP-1 and HNP-2 (page 2937, figure 2), said defensins having molecular weights of 3.45 and 3.38 kDa, respectively, which fulfill the limitation of claim 42. The defensins of Chertov et al meet the limitations of the product by process claims of 43 and 44 because the product is the same as the product purified by the claimed method.

Claims 1, 2, 4-8, 25, 26, 32 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Fung et al (Current Opinion in Molecular Therapeutics, 2000, Vol. 2, pp. 643-650).

Fung et al teach the differential detection by SELDI mass spectrometry of a markers having masses of 3448, 4036 and 8445 in the seminal plasma of cancer patients versus healthy age-matched individuals (all of page 648, ,and figure 1).

Claims 1-8, 10, 11, 24-27, 32, 36, 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Pawletz et al (Drug Development Research, 2000, Vol. 49, pp. 34-42).

Pawletz et al disclose a method for detecting the EP12 marker comprising using SELDI-mass spec with laser capture microdissected tumor cells including prostate tumor cells (page 40, figure 4). It appears that peak "A" has the same molecular weight as the instant marker EP12, and differentially expressed in normal versus neoplastic or tumor cells (Figure 4B). When given the broadest reasonable interpretation, LCM separation of cells fulfill the limitations of "fractionating the sample" in claims 10 and 31.

Claims 1-11, 24-29, 31-46 is rejected under 35 U.S.C. 102(e) as being anticipated by Wright et al (WO 01/71360, reference of the IDS filed Nov., 9, 2005).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Wright et al disclose a marker having a mass/charge ratio of 8,494.30 Da plus or minus 10.24 Da present in cells isolated in LCM from prostate tumors which fulfills the embodiments of the instant claims with respect to the EP9 marker of 8445 Da plus or minus 46 Da.. Wright et al disclose all other particular elements of the instant claims including the SELDI using antibodies, hydrophilic absorbent comprising silicon dioxide, or copper, differential expression of the marker and kits comprising the marker.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25-41 are rejected under 35 U.S.C. 103(a) as being obvious over Wright et al (WO 01/71360) in view of Hitt et al (WO02/006829).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C.

102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claim 30 embodies the method of claim 29 wherein the artificial intelligence program is a fuzzy logic, cluster analysis or neural network.

Wright et al teach that the algorithm provides for a closeness of fit of the data to PCA, PIN or BPH. Wright et al do not specifically teach the specific algorithm for data reduction.

Hitt et al teach cluster analysis and fuzzy mapping as methods of deconvuluting biological data.

It would have been prima facie obvious at the time the claimed invention was made to use the algorithms of Hitt et al in the determination of PCA, PIN or BPH in the method of Wright et al. One of skill in the art would have been motivated to do so by the specific teachings of Hitt et al in how to discriminate between biological states based on patterns in biological data.

Claims 25, 26, 29, 30, 32 and 37 rejected under 35 U.S.C. 103(a) as being unpatentable over Fung et al (Current Opinion in Molecular Therapeutics, 2000, Vol. 2, pp. 643-650).

Fung et al teach the differential detection by SELDI mass spectrometry of a markers having masses of 3448, 4036 and 8445 in cancer patients versus healthy age-matched individuals (all of page 648, ,and figure 1). Fung et al suggests that proficiency and accuracy with the diagnostic approach require further development of pattern matching, artificial intelligence

software, such as fuzzy logic, cluster analysis, neural networks or other algorithms that incorporate bioinformatics and bio-statistical analysis (page 648, second column, lines 6-15).

It would have been prima facie obvious at the time the claimed invention was made to use algorithms such as fuzzy logic, cluster analysis and neural networks in order to apply the protein patterns discerned by the SELDI technique to the accurate diagnosis of PCA, PIN, BPH or normal. One of skill in the art would have been motivated to do so by the suggestion of Fung et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 25-27, 31-46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 10/381,369. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '369 patent anticipate the instant claims to the extent that they are drawn to compositions and methods using Marker UBC-1 characterized by a molecular weight of 3432 Da plus or minus 122 Da and 3470 Da plus or minus 32 Da which is the same as the instant marker EP1 having a molecular weight of 3448 Da plus or minus 19 Da.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 2, 4-6, 25, 26, 32, 36-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-54 of copending Application No. 10/088,970. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are obvious over the claims of the '970 application as all the biomarker of the instant application have masses less than 10,000 Da.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

All claims are rejected.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Wright et al (Prostate Cancer and Prostatic diseases, 1999, vol. 2, pp. 264-276).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A. Canella/
Ph.D., Primary Examiner
Art unit 1643